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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,077	ERBE ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-43,63-71 and 73-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-43,63-71 and 73-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Amendments to claims 32, 41, 69, 71, and 73-77 have been entered. Claims 1-31, 44-62, and 72 have been cancelled. Claims 32-43, 63-71 and 73-78 remain pending in the current application.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: BIOCOMPATIBLE BONE GRAFT MATERIAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 71 and 73-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 71 is directed to a graft for the restoration of bone in the form of a shaped body, the shaped body comprising a homogenous composite of polymer and β-tricalcium phosphate, the graft having interconnected macro-, meso-, and microporosity; the shaped body being selected to conform generally to a mammalian, anatomical tissue structure; and further comprising a mesh affixed to a side of the composite.

It is unclear how a composite of polymer and β-tricalcium phosphate is to be homogeneous. A homogeneous mixture would uniform throughout, implying a single component, not a composite of two

or more. In fact, the word 'composite' means 'comprising distinct parts.' The term appears to be an oxymoron.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 63 stands rejected under 35 U.S.C. 102(b) as being anticipated by Sapiesko et al (US Patent 6,383,519).

Sapiesko et al teach porous, shaped, inorganic bodies comprising biocompatible, resorbable polymers, such as gelatin, and the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent and at least one oxidizable precursor anion (See col. 4, ln 3-34). In preferred embodiments the oxidation-reduction reaction product is beta tricalcium phosphate (See col. 8, ln 28-46). The composition of Sapiesko et al can be used as bone graft material (See col. 5, ln 7-9). The bone graft material of Sapiesko et al exhibits macro-, meso- and microporosity, and the material has a pore volume of at least 75% (See col. 9, ln 39- col. 10, ln 25) (Claim 63). The graft material can be formed into a variety of shapes, including blocks, disks, cylinders, or sleeves for orthopedic surgery (See col. 12, ln 1-13; col. 23, ln 63-65; col. 42, ln 64-67) (Claim 63). Therefore the reference anticipates the claimed subject matter.

Response to Arguments

Applicant argues that Sapiesko et al do not teach a graft material having interconnected macro-, meso-, and microporosity comprising a polymer and β-tricalcium phosphate, rather there are only bodies that can be "reinforced with polymers" but no showing that the reinforced bodies maintain their porosity.

Applicant's arguments are not found persuasive because Sapiesko clearly teaches that the shaped bodies retain their porosity after being reinforced with polymers, as evidenced by "...the invention also

gives rise to **porous inorganic composites** comprising mineral scaffolds strengthened and/or reinforced with polymers, especially film-forming polymers such as gelatin."(Sapiesko, col. 4, ln 31-34). Sapiesko et al clearly define the end product as a **porous inorganic composite** (which applicant calls a bone graft), thus mineral scaffold reinforced with polymers produces a porous graft. Sapiesko et al further characterize the porosity as a combination of macro-, meso-, and microporosities, wherein the graft can have a pore volume greater than 90% (See col. 9, ln 39-col. 10, ln 25); one skilled in the art that in a graft with a pore volume of greater than 90% the pores are inherently interconnected. Therefore Sapiesko et al, do in fact, teach every limitation of claim 63.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-40, 63, 67-70 and 74-78 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Piez et al (US Patent 4,795,467), in light of Bachand.

Piez et al teach bone grafts comprised of calcium phosphate mineral preparations (which applicant calls the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion) and collagen (which applicant calls a biocompatible, resorbable polymer) (See col. 2, ln 32-35). The calcium phosphate mineral material can include a variety of forms of calcium phosphate, including beta tricalcium phosphate SYNTHOGRAFT; SYNTHOGRAFT is a commercially available form of beta tricalcium phosphate (See col. 2, ln 59-68 & Bachand, Pg. 2). The collagen is preferably obtained from the same individual or from bovine sources in order to reduce immune responses and increase biocompatibility (See col. 1, ln 30-35). Piez et al also teach a method for

restoring or repairing bone comprising placing into a bony space the bone graft material comprised of calcium phosphate and collagen (See col. 2, ln 48-52, col. 5, ln 23-35 & col. 7, ln 4-48). Additionally, Piez et al teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2).

Piez et al teach the mineral blocks, made from powdered tricalcium phosphate or hydroxyapatite, used to form the bone grafts to be porous (See col. 5, ln 36-43); however, they do not specifically teach the bone grafts to have macro-, meso- or microporosity. The size range of the pores is a result effective variable that would routinely be optimized by one of ordinary skill in the art. Piez et al clearly indicate that the mesh size of the tricalcium phosphate and/or hydroxyapatite particles used in the claimed composition directly effects the size of the pores (See col. 5, ln 63-68). Therefore, it would have been obvious to one of ordinary skill in the art to use a mineral particles with varied mesh sizes in order to achieve macro-, meso- and microporosity in the bone graft material of Piez et al, as described above (Claims 32, 39, 63, 67, 71 and 74). One of ordinary skill in the art would have been motivated to use mineral particles with varied mesh sizes in order to create a mineral block, for use in a bone graft, with macro-, meso- and microporosity, in order to better replicate natural, porous bone structure for bone and blood cells to invade. One would have expected success because Piez et al teach a method for producing mineral blocks from particles of beta tricalcium phosphate and/or hydroxyapatite and collagen, and coating the mineral blocks in collagen to produce bone graft materials and Piez et al teach that the mesh size of the mineral particles directly effects the resulting pore size; therefore because pore size is a result effective variable, one would have expected success creating macro-, meso- and microporosity by using particles of varied mesh size.

Piez et al teach the bone graft composition should comprise approximately 75-98% by weight calcium phosphate mineral component and approximately 25-2% by weight collagen (See col. 4, ln 57-65). In example 1, Piez et al produce bone graft material by combining 65% hydroxyapatite with 35%

collagen; hydroxyapatite was used in place of tricalcium phosphate, as Piez et al teach either mineral can be used (See col. 7, ln 4-48 & col. 2, ln 32-40). Piez et al use ZYDERM collagen, which is 6.5% collagen in saline; therefore the final bone graft composition is 2.3% collagen by weight (Claims 36-38). However, it would have been obvious to one of ordinary skill in the art to develop the bone graft material of Piez et al using anywhere between 75-98% by weight beta tri-calcium phosphate (i.e. SYNTHOGRAFT) and 2-25% collagen (mass ratio of beta-tricalcium phosphate and collagen is (75-98):(25-2); therefore the mass ratio can be 70:30, 80:20 or 90:10) (Claim 34). Piez et al teach that the ratio of calcium phosphate to collagen is a direct result of the mesh size of the mineral particles used; the particle size directly effects the level of porosity, and therefore the amount of collagen that fills the pores. Larger mesh size creates more pore space, and therefore a greater amount of collagen present in the graft. The mesh size of the mineral particles is a result effective variable that would routinely be optimized by one of ordinary skill in the art to obtain the desired calcium phosphate to collagen ratio (See col. 5, ln 63-68). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to alter the mesh size of the particles to create bone grafts with calcium phosphate to collagen ratios of 70:30, 80:20 or 90:10 (Claims 35-38, 68-69 and 77-78). One of ordinary skill in the art would have been motivated to manipulate the mesh size of the mineral particles in order to increase or decrease the ratio of calcium phosphate to collagen in order to alter the rigidity of the graft material, within the range of about 75-98% by weight calcium phosphate mineral component and about 25-2% by weight collagen, as taught by Piez et al. For example, one of ordinary skill in the art would desire a high calcium phosphate to collagen ratio in order to produce a more rigid graft material, for graft use in long bones or other load bearing bone grafts. A lower calcium phosphate to collagen ratio would be desirable in grafts where load bearing capabilities are not immediately necessary, for instance cranial grafts do not need to be able to withstand the weight of the body, rather a higher amount of resorbable collagen would be tolerable, then the resorbable collagen would eventually be replaced with a greater number of natural

bone cells. One would have expected success because Piez et al teach that the ratio of calcium phosphate to collagen can be routinely optimized by one of ordinary skill in the art by manipulating the mesh size of the mineral particles (See col. 5, ln 63-68).

Though Piez et al teaches the collagen can come from a bovine source, they do not teach a specific kind or concentration of any particular type of bovine collagen. However, they do teach that purified atelopeptide fibrillar reconstituted collagen is suitable for their bone graft material (See col. 4, ln 41-42). Piez et al also teach type I collagen, derived from bones, is the most common type of collagen, and they teach a method to remove the telopeptides from common collagen to produce "atelopeptides." (See col. 3, ln 17-col. 4, ln 15). Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use fibrillar type I bovine collagen in the bone graft material of Piez et al because Piez et al teach bovine collagen has low immune response when used in humans, they teach type I collagen is the most common type of collagen, easily found in bone sources, and Piez et al teach a method using proteolytic enzymes to remove the telopeptides from type I collagen to produce the desired "atelopeptide" collagen used in their material (Claim 33). It would further have been obvious to one of ordinary skill in the art at the time the invention was made to use substantially pure fibrillar type I bovine collagen, and therefore at least 85% type I bovine collagen, in order to prevent impurities that may cause immunologic reactions. One of ordinary skill in the art would have been motivated to use at least 85% type I bovine collagen as the collagen source because Piez et al teach that bovine collagen has low immune response when used in humans, and they teach that type I collagen, derived from bones, is the most common type of collagen; therefore substantially pure type I bovine collagen would be easy to obtain. One would have expected success because Piez et al teach that atelopeptide fibrillar collagen is suitable for use in the bone graft material, and they provide a method to remove the telopeptides.

Piez et al do teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2); however, it

would have been obvious to one of ordinary skill in the art at the time the invention was made to form the graft into any desired shape, including a cylinder, disk, a sleeve shape or a half sleeve shape, wherein the cross section of the sleeve is in the shape of a crescent moon, semi-sphere, semi-tubular, torus, or in a shape to conform to the acetabulum or any other desired anatomical tissue structure (Claims 40, 63, 70, 75 and 76). One of ordinary skill in the art would have been motivated to form the bone graft material of Piez et al into any desired shape, including those listed above, in order to better fit the bone graft to the osseous void it will be engrafted to. For example, a semi-sphere shaped graft would be more desirable for replacing or repairing a rotator cup on a shoulder than a flat disk. One would have expected success forming the bone graft of Piez et al into any desired shape because Piez et al teach their bone graft can be made by pouring a slurry of the mixture of the collagen and calcium phosphate component into an appropriate container, wherein upon solidification the bone graft takes the form of the container; therefore the bone graft can be made into any shape that a container can be molded into. One skilled in the art would be able to make, or obtain, a mold in any desired custom-made shape.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 41-43, 63-66, 71 and 73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Piez et al (US Patent 4,795,467), in light of Bachand, in view of Koblish et al (US Patent 6,458,162), and further in view of Lin et al (US Patent 6,458,162) and Sanders et al (US Patent 5,290,289).

Piez et al teach bone grafts comprised of calcium phosphate mineral preparations (which applicant calls the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent, and at least one oxidizable precursor anion) and collagen (which applicant calls a biocompatible, resorbable polymer) (See col. 2, ln 32-35). The calcium phosphate mineral material can include a variety of forms of calcium phosphate, including beta tricalcium phosphate SYNTHOGRAFT; SYNTHOGRAFT

is a commercially available form of beta tricalcium phosphate (See col. 2, ln 59-68 & Bachand, Pg. 2). The collagen is preferably obtained from the same individual or from bovine sources in order to reduce immune responses and increase biocompatibility (See col. 1, ln 30-35). Piez et al also teach a method for restoring or repairing bone comprising placing into a bony space the bone graft material comprised of calcium phosphate and collagen (See col. 2, ln 48-52, col. 5, ln 23-35 & col. 7, ln 4-48). Piez et al teach bone marrow, blood and saline can also be applied to the graft material (See col. 5, ln 15-21). Additionally, Piez et al teach the graft material can be loaded into a container to provide a desired shape, Piez et al specifically teach block, square, and sheet shapes (See col. 4, ln 67-col. 5, ln 2).

Piez et al teach that the mesh size of the mineral particles is a result effective variable that directly effects the degree of porosity, the pore volume, and the ratio of collagen to reaction product. Therefore it would have been obvious to one of ordinary skill in the art to develop mineral particles of appropriate sizes to provide the bone graft material with macro-, meso- or microporosity, at least 70% porosity and for at least 80% of the composition to comprise calcium phosphate (e.g. 80:20 or 90:10 calcium phosphate to collagen mass ratios). See teachings above.

Though Piez et al teaches the collagen can come from a bovine source, they do not teach a specific kind or concentration of any particular type of bovine collagen. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use at least 85% fibrillar, reconstituted type I bovine collagen in the bone graft material of Piez et al. See teachings above.

Piez et al do teach the graft material can be loaded into a container to provide a desired shape, therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to form the graft into any desired shape, including a cylinder, disk, a sleeve shape or a half sleeve shape, wherein the cross section of the sleeve is in the shape of a crescent moon, semi-sphere, semi-tubular, torus, or in a shape to conform to the acetabulum or any other desired anatomical tissue structure. See teachings above.

Piez et al do not teach their graft to further comprise a mesh or plate comprised of a metal or polymer. However, Koblish et al teach a similar bone graft material comprising porous calcium phosphate that can be formed on, around, or immersed within a solid material, such as metal or polymers (See Koblish et al, col. 26, ln 56-col. 27, ln 57). The metals and/or polymer material provides support and increased structural integrity, especially in load-bearing grafts, such as in the spinal vertebrae. Suitable metals include stainless steel, titanium, silver, gold and other metals stable in the human body (See col. 27, ln 1-3) (Claims 41, 42, 66, 71 and 73).

Though Koblish et al do not teach nitinol or polyetheretherketone as possible materials for the metal or polymer material, it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use nitinol or polyetheretherketone as the metal or polymer material. One of ordinary skill in the art would have been motivated to use polyetheretherketone as the supporting material in the grafts of Koblish et al because Lin et al teach PEEK to have excellent mechanical properties and machinability, and PEEK materials have been shown to be suitable for implantation (See Lin et al, col. 5, ln 38-52). Similarly, one of ordinary skill in the art would have been motivated to nitinol as the supporting material in the grafts of Koblish et al because Sanders et al teach that nitinol is especially suitable for implantation and has particular applicability in augmenting or restoring damaged spinal vertebrae that are misshaped, due to its ability to "remember" its designated shape (See Sanders et al, col. 4, ln 13-47). One would have expected success using either PEEK or nitinol as the metal material in the graft of Koblish et al because Koblish et al teach that any metal stable in the human body can be used, and Lin et al and Sanders et al teach that PEEK and nitinol, respectively, are suitable for use in human implantation.

Though Koblish et al do not describe a mesh composite, it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use a mesh material in place of a solid material. One of ordinary skill in the art would have been motivated to use a mesh material in

order to allow for less restricted flow of biological materials, such as osteocytes and blood flow into and out of the graft. One would have expected success because a strong mesh would provide similar support as solid material, and one of ordinary skill in the art would know how to perform such substitution.

It would have further been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the metal or polymer mesh or plate of Koblish et al, which can be modified in view of Lin et al or Sanders et al to comprise PEEK or nitinol material, into the bone graft of Piez et al in order to improve structural stability and provide additional support to the bone graft of Piez et al. The skilled artisan would have been motivated to add a metal or polymer mesh or plate component to the bone graft of Piez et al in order to provides support during development of the bone graft, and to provide increased stability and structural integrity to the bone graft after implantation. One would have been motivated to have the mesh or plate immersed within the bone graft of Piez et al when the bone graft is large in size, for example, in long bone grafts (Claim 65). Similarly, one would have been motivated to affix the mesh to the surface of a sleeve shaped graft in order to maintain structural integrity once implanted (Claim 64). One would have expected success applying the metal or polymer plate or mesh of Koblish et al to the grafts of Piez et al because both grafts are made from substantially similar materials in similar methods, and Koblish et al teach successful incorporation of the metal or polymer supports to the grafts; therefore one would expect similar success performing the same incorporation of the metal or polymer grafts into the grafts of Piez et al.

Finally, it would have further been obvious to one of ordinary skill in the art at the time the invention was made to shred the graft material of Piez et al (Claim 43). One would have been motivated to shred the graft material of Piez et al in order to fill a metal or polymer body housing, such as those described by Koblish et al, with the bone graft shreds. By shredding the bone graft material one can increase the pore volume of the graft, therefore allowing for increased pore volume for ingrowth of autogenous bone and blood cells. Filling a housing with shredded bone grafts provides a prosthesis with

the appropriate bone graft material, but wherein the structural integrity comes exclusively from the housing. Shredding the bone graft material and depositing the shreds in a solid housing would be a desirable means to utilize pieces of left over bone graft materials that are not large enough to act as a complete, solid graft, but rather can be shredded and packed in housing. One would have expected success because shredding the bone graft material of Piez et al could be done by such simple methods as processing left over pieces in a blender.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 70 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Sapiesko et al (US Patent 6,383,519).

Sapiesko et al teach a porous, shaped, inorganic bodies comprising biocompatible, resorbable polymers, such as gelatin, and the oxidation-reduction reaction product of at least one metal cation, at least one oxidizing agent and at least one oxidizable precursor anion (See col. 4, ln 3-34). In preferred embodiments the oxidation-reduction reaction product is beta tricalcium phosphate (See col. 8, ln 28-46). The composition of Sapiesko et al can be used as bone graft material (See col. 5, ln 7-9). The bone graft material of Sapiesko et al exhibits macro-, meso- and microporosity, and the material has a pore volume of at least 75% (See col. 9, ln 39- col. 10, ln 25). The graft material can be formed into a variety of shapes, including blocks, disks, cylinders, or sleeves for orthopedic surgery (See col. 12, ln 1-13; col. 23, ln 63-65; col. 42, ln 64-67).

Sapiesko et al teach the bone graft material can be custom tailored based on the absorbent material chosen as the initial support or by custom carving a desired shape out of a large block of the graft material (See col. 12, ln 25-30 and 42, ln 64-67); therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to form grafts in the shape of sleeves, wherein the cross-

section of the sleeve is in the shape of a crescent moon, or shapes selected to conform to mammalian, anatomical tissue structure, for example in the shape of a semi-sphere, semi-tubular, or torus (Claim 70). One of ordinary skill in the art would have been motivated to custom tailor the grafts of Sapiesko et al into any desired shape, including those listed above, in order to better fit the bone graft to the osseous void it will be engrafted into/onto. For example, a semi-sphere shaped graft would be more desirable for replacing or repairing a rotator cup on a shoulder than a flat disk. One would have expected success forming the bone graft of Sapiesko et al into any desired shape because Sapiesko et al teach the shape of the bone graft is determined by the shape of the absorbent material chosen as the initial support. In their examples Sapiesko et al use materials as pliable as kitchen sponges; one of ordinary skill in the art would be able to manipulate the shape of these initial support materials, either by placing in a mold or by cutting, to the desired shapes, including sleeves, wherein the cross-section of the sleeve is in the shape of a crescent moon, or shapes selected to conform to mammalian, anatomical tissue structure, for example in the shape of a semi-sphere, semi-tubular, or a torus.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 26 August 2005 have been fully considered, but are not found persuasive. In particular applicant's argue that the Bachand document is not mentioned in a substantive portion of the rejection of the claims; additionally, applicants state that no publication date was provided for the Bachand reference, and thus it is impermissible as 103(a) art. Applicant further argues that it would not have been obvious to one skilled in the art to use mineral particles with varied mesh sizes to produce the claimed bone grafts having macro-, meso-, or microporosity. Applicants state the motivation provided by the examiner was flawed, as Piez teaches a pore size range of 100-2000um, as compared to

applicant's pore diameters of as low as 10um; thus applicants argue Piez et al teaches away from the instantly claimed invention. Applicant also argues that there is no evidence that once the porous graft of Piez et al is imbibed with the collagen polymer that it retains its porosity. Still further, applicant argues that proper motivation has not been provided for the combination of Piez et al and Koblish et al. Additionally applicants state the supporting obvious rationale statements made by the examiner are conclusory statements of generalized advantages and convenient assumptions about the state of the art and are inadequate to support a finding of motivation, citing *In re Lee*. Applicants appear to further argue the Koblish patent specifically teach away from the use of mesh materials.

With regards to the Bachand document, the examiner concedes that it was not used in a substantive portion of the rejection of the claims, rather the examiner merely relied on the Bachand document to provide a definition of the components of SYNTHOGRAFT. In the Piez et al patent the use of SYNTHOGRAFT is described (See Piez, col. 2, ln 59-68); Bachand merely defines the commercially available SYNTHOGRAFT to comprise β-tricalcium. Thus, Bachand was not relied on as a showing of prior art, but rather to provide a definition. The Bachand document was retrieved from the internet at http://das.cs.amedd.army.mil/journal/J9712.HTM, it was retrieved on 4 March 2005, as indicated on the PTO-892. For electronic documents retrieved off the internet it is only required that the date of retrieval be provided, see MPEP § 707.05(e) IV (B). Therefore, the use of the Bachand document to define the composition of SYNTHOGRAFT is deemed permissible.

In response to applicant's arguments that it would not have been obvious to use mineral particles with varied mesh sizes to produce the claimed bone grafts it is noted that applicants define microporosity as less than about 10um, and Piez et al teach a pore size range of only 100-2000um; however the examiner maintains that it would have been prima facie obvious to modify the mineral particle mesh size in order to create a bone graft material with a greater range of pore sizes in order to better replicate the natural, varied porosity of real bone. Piez et al teach that pore size is a result effective variable that is

directly affected by the mesh size of the mineral particles chosen (See Piez et al, col. 5, ln 63-68); result effective variable are routinely optimized by those of ordinary skill in the art. Additionally, in the instant case the range disclosed by Piez et al overlaps with that disclosed by applicant, it is well established in patent law that where the claimed ranges overlap or lie inside ranges disclosed by the prior art a prima facie case of obviousness exists, see *In re Wertheim, 541 F.2d 257, 191USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir. 1990),* especially in the lack of evidence showing unexpected results at the points (in this case pore sizes) outside the range disclosed by the prior art. Regarding Piez et al allegedly 'teaching away' it is noted that though Piez et al do not specifically teach pore sizes of with diameters of less than about 10um, they do not teach or suggest negative results when such small diameters are used. A reference merely not teaching every limitation does not constitute teaching away by that reference. See *In re Grasselli* 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983). Finally, applicant refers to the Sapiesko patent as evidence of how the prior art shows that one skilled in the art would not achieve macro-, meso-, or microporosity by compressing particles together as taught by the Piez et al patent; this argument is unclear as there is no specific points or teachings provided from the Sapiesko patent to support this assertion.

In response to applicant's argument that no showing has been provided that the Piez et al graft maintains its porosity after being imbibed with the polymer, it is noted that applicant has provided no showing or evidence to the contrary. While Piez et al do teach that the collagen gel is limited to the void space between the HA particles, one of ordinary skill in the art would recognize that the degree of saturation of the pores depends on the amount of collagen gel added. It would be well within the purview of one skilled in the art to modify the amount of collagen gel so that the collagen does not completely fill the pores, but rather provides a coating for improved adhesion and invasion of natural cells, yet allows room for cell multiplication and growth. This argument appears to be merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Counsel's arguments cannot take

the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964): and especially *In re Langer*, 183 USPQ 288 (CCPA 1974).

In response to applicant's argument that there is no suggestion to combine the Piez et al and Koblish references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the examiner did not intend to state Koblish taught the claimed bone graft material, but rather that Koblish et al taught a synthetic bone graft material for natural bone repair that could be improved by metal support. The examiner relied on the combination of the teachings of Koblish et al and Piez et al, wherein the metal support of Koblish et al could be modified to improve the bone graft of Piez et al. Though Koblish et al teach solid materials were desired for their applications the examiner has provided motivation for modifying the solid material of Koblish et al into a mesh-like material for use with the bone graft of Piez et al. Specifically, one of ordinary skill in the art would have been motivated to use a mesh material in order to allow for less restricted flow of biological materials, such as osteocytes and blood flow into and out of the graft. Also, though Koblish found spongiform materials less desirable than solid counterparts for their particular applications, there is no evidence that such mesh composites would be undesirable in the separate applications of Piez et al. In fact, mesh composites would provide added support, but allow for ingrowth of blood vessels and natural osteocytes without inhibition in the graft material of Piez et al. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use. *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Additionally, please note that the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly

contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. See MPEP §2144.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available

through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER